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# INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification <sup>6</sup>:

C12N 15/53, 15/86, A61K 48/00

A3

(11) International Publication Number: WO 95/12678

(43) International Publication Date: 11 May 1995 (11.05.95)

(21) International Application Number:

PCT/GB94/02423

(22) International Filing Date:

4 November 1994 (04.11.94)

(30) Priority Data:

9323008.4

5 November 1993 (05.11.93) GB

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(81) Designated States: AU, CA, JP, NZ, US, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

#### Published

With international search report.

Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(88) Date of publication of the international search report:
15 June 1995 (15.06.95)

- (54) Title: IMPROVEMENTS RELATING TO CANCER THERAPY
- (57) Abstract

The system of the invention comprises: (i) a viral vector comprising a nucleotide sequence encoding a nitroreductase, which nitroreductase in capable of converting a prodrug into a cytotoxic drug; and (ii) a prodrug capable of being converted into a cytotoxic drug by the nitroreductase encoded by the vector.

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tational Application No PCT/GB 94/02423 A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/53 C12N15/86 A61K48/00 According to International Patent Classification (IPC) or to both national classification and IPC B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) IPC 6 A61K C12N Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) C. DOCUMENTS CONSIDERED TO BE RELEVANT Category \* Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. X EP,A,O 330 432 (THE DEPARTMENT OF 12 MOLECULAR PHARMACOLOGY, INSTITUTE OF CANCER RESEARCH) 30 August 1989 see column 3 and 7 12 X EP,A,O 540 263 (CANCER RESEARCH CAMPAIGN TECHNOLOGY LIMITED) 5 May 1993 see pages 4-6 see the whole document 1-11,13-17 Further documents are listed in the continuation of box C. Patent family members are listed in annex. Special categories of cited documents: "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the "A" document defining the general state of the art which is not considered to be of particular relevance 'E' earlier document but published on or after the international "X" document of particular relevance; the claimed invention filing date cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such docudocument referring to an oral disclosure, use, exhibition or ments, such combination being obvious to a person skilled document published prior to the international filing date but later than the priority date claimed '&' document member of the same patent family Date of the actual completion of the international search Date of mailing of the international search report

European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016 Form PCT/ISA/210 (second sheet) (July 1992)

Name and mailing address of the ISA

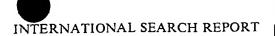
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,			
	BIOCHEM.PHARMACOL., vol.44, no.12, 15 December 1992, ENGLAND pages 2289 - 2295 ANLEZARK, G.M. ET AL. 'The bioactivation of 5-(aziridin-1-yl)-2,4-dinitrobenzamide (CB1954)I. Purification and properties of a nitroreductase enzyme from Escherichia coli a potential enzyme for antibody-directed enzyme prodrug therapy (ADEPT)'	·	12
Y	see Figure 1 see whole document		1-11, 13-17
Y	PROC.NATL.ACAD.SCI., vol.88, September 1991, USA pages 8039 - 8043 HUBER, B.E. ET AL. 'Retroviral-mediated gene therapy for the treatment of hepatocellular carcinoma: An innovative approach for cancer therapy' see page 8040, left-hand column, lines 6-25 to right-hand column, lines 1-14; page 8043, right-hand column, last paragraph		1-11, 13-17
<b>Y</b> .	PROC.NATL.ACAD.SCI., vol.89, 1992, USA pages 33 - 37 MULLEN, C.A. ET AL. 'Transfer of the bacterial gene for cytosine deaminase to mammalian cells confers lethal sensitivity to 5-fluorocytosine: a negative selection system'		1-11, 13-17
		٠.	
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PCT/GB 94/02423

Patent document cited in search report	Publication date	Patent memb		Publication date
EP-A-0330432	30-08-89	AU-A- EP-A- WO-A- JP-T-	3439889 0429454 8907592 3503761	06-09-89 05-06-91 24-08-89 22-08-91
EP-A-0540263	05-05-93	AU-A- EP-A- WO-A- JP-T-	2776992 0638123 9308288 7501692	21-05-93 15-02-95 29-04-93 23-02-95